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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,548	12/12/2003	Shyam S. Mohapatra	USF-T187XC1	4609

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

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09/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,548	MOHAPATRA ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 21-30* is/are pending in the application.

4a) Of the above claim(s) *4-6,12 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-11,13 and 21-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on August 21, 2007.

Currently, claims 1-13 and 21-30 are pending in the instant application. Applicant added new claims, claims 28-30, which are not directed to the originally elected invention. Note that applicant elected without traverse claims 21-27 comprising administering an siRNA. The new claims, claims 28-30, on the other hand, are drawn to a method comprising administering a 5-50 nucleotide-long oligonucleotide that is complementary to PKC mRNA. See applicant's election filed on February 27, 2007. Therefore, claims 28-30 are withdrawn from further consideration as being drawn to a non-elected invention. Accordingly, claims 1-3, 7-11, 13, and 21-27 are under examination on the merits.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

Claims 1-3, 7-11, 13, and 21-27 remain rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement for the reasons of record as set forth in the Office action mailed on March 21, 2007 and for the reasons stated below.

Applicant's arguments filed on August 21, 2007 have been fully considered but they are not persuasive. Applicant argues that the specification discloses many chemical PKC inhibitors and that various oligonucleotide inhibitors of PKC are known in the art such as the antisense oligonucleotide PKC inhibitor of Bennet et al., which is shown to treat cancer *in vivo*. Although applicant is correct that the existence of PKC chemical inhibitors and PKC antisense oligonucleotides was known in the art, no PKC inhibitors, whether chemical or oligonucleotide, were known to inhibit RSV infection in a mammal *in vivo*, which is the claimed invention in the instant case. Furthermore, the specification discloses no species that is capable of inhibiting RSV infection in a mammal *in vivo,* wherein the species is a PKC inhibitor. The specification provides only a single species for the claimed genus of PKC inhibitors that inhibit RSV infection when introduced into cultured cells *in vitro,* which is the chemical compound RO318220.

Note that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the

disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]." See *Enzo Biochem*, 323 F.3d at 966, 63 USPQ2d at 1615; *Noelle v. Lederman*, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). See also MPEP §2163.

In light of the above, the instant specification, which is silent about any species that is representative of the claimed PKC inhibitors that treat RSV infection *in vivo,* does not clearly allow persons of ordinary skill in the art to recognize that the inventors invented the genus claimed in the instant case. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991), which clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (see page 1117). In the instant case, applicant failed to convey with reasonable clarity that applicant was in possession of a pharmaceutical PKC inhibitor that treats RSV infection when administered *in vivo* into a mammal including human, let alone the claimed species of pharmaceutical siRNA compound targeted to PKC. Accordingly, this rejection is maintained.

Claims 1-3, 7-11, 13, and 21-27 remain rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement for the reasons of record as set forth in the Office action mailed on March 21, 2007 and for the reasons stated below.

Applicant's arguments filed on August 21, 2007 have been fully considered but they are not persuasive. Applicant argues that the data in the Examples of the specification establish the fundamental concept of the invention such that PKC inhibition "would be of benefit in inhibiting RSV infection". Applicant further asserts that the state of the art was "sufficiently developed" and tools and method for achieving the required PKC inhibition were "available to those of ordinary skill in the art". In support of applicant's assertions, applicant lists references and documents, stating that a large variety of PKC inhibitors such as chemical agents, antisense oligonucleotides, and siRNAs were known in the art, wherein some references "describe gene silencing using interfering RNA *in vivo*".

In an effort to overcome the enablement rejection, applicant submitted only counsel's arguments without supporting evidence such as declaration filed under 37 CFR 1.132. Applicant's attention is directed to MPEP §2164, which teaches, "it must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. For example, in a case where the record consisted substantially of arguments and opinions of applicant's attorney, the court indicated that factual affidavits could have provided important evidence on the issue of enablement."

Applicant has submitted post-filing references, some of which are published in the year of 2007. The claims were examined under 35 U.S.C. 112, first paragraph as of the earliest filing date granted in the instant application, which is December 12, 2003. That is, the claimed methods of treating RSV infection in human comprising administering an siRNA molecule targeted to PKC alpha mRNA via nasal or oral administration wherein the siRNA molecule is

delivered to bronchial epithelium were not enabled as of December 12, 2003, as evidenced by the fact that no correlation between reduction in PKC alpha mRNA expression *in vivo* and inhibition of RSV infection *in vivo* was provided by either the instant specification or the prior art references. The lack of correlation together with the unpredictable pharmacokinetics of siRNA molecules recognized in the art as of December 12, 2003 would have necessitated undue experimentation for one of ordinary skill in the art to practice the claimed therapeutic methods. The content of the instant specification (lack of *in vivo* working examples comprising anti-PKC siRNA molecule administered nasally or orally into a mammal with a resultant effect of inhibiting RSV infection in the mammal) provides no appropriate and specific guidance that is commensurate in scope with the claimed invention. See Examples 1-6 disclosed in the specification, none of which demonstrates even a single aspect of the claimed therapeutic methods. Example 6 discusses "gene therapy" approaches for treating RSV infection; however, it is entirely prophetic as well as generic, and furthermore, its content is devoid of inventor's working examples or specific guidance directed to the instantly claimed methods. It is true that the instant specification contains the term "siRNA"; nevertheless, this term appears twice in brief description of the invention without any further elaboration. See page 8: "In addition, PKC antisense or plasmids encoding siRNA that targets PKC, which can be complexed with nanoparticles specifically addressed to bronchial epithelium (a primary target for RSV infection), can also be used." See also page 27, which basically repeats the statement written on page 8: "In addition, plasmid encoding PKC regulatory domains or siRNAs complexed with nanoparticles targeting specific cell types (such as bronchial epithelium) can be used." As the term "siRNA" is not merely a term but is an essential subject matter in the instant case, the mere appearance of the

term "siRNA" in the two prophetic sentences in the specification does not satisfy the enablement requirement under 35 U.S.C. 112, first paragraph.

With regard to disclosing working examples, MPEP 2164.02 teaches that "Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art." Note that "if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling." . MPEP 2164.02 further teaches that an *in vitro* or *in vivo* animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention. If there is no correlation, then the examples do not constitute "working examples."

See also *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) which teaches the following: "Nascent technology, however, must be enabled with a ***"specific and useful teaching"***. The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology." (original emphasis)

Since the amount of guidance or direction needed to enable the invention is ***inversely*** related to the amount of knowledge in the state of the art as well as the predictability in the art, and since RNAi technology directed to treating RSV infection in a mammal including human by targeting endogenous PKC expression level was underdeveloped and therefore considered as nascent technology as of the earliest filing date sought in the instant application, and since there is no enabling disclosure pertaining to RSV treatment in a mammal comprising administering a

PKC inhibitor regardless of the type of inhibitor, it is reasonably concluded that, in view of the totality of the factors listed above and the evidence/arguments provided by applicant, the specification fails to comply with the enablement requirement, thereby necessitating undue experimentation for one of ordinary skill in the art to practice the claimed *in vivo* methods in mammals.

See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991), wherein the Court ruled that a rejection under 35 U.S.C. 112, first paragraph for lack of enablement was appropriate given the relatively incomplete understanding in the biotechnological field involved, and the lack of a reasonable correlation between the narrow disclosure in the specification and the broad scope of protection sought in the claims.

In view of the above, it is concluded that the instantly claimed invention failed to comply with the enablement requirement, thus necessitating undue experimentation for one of ordinary skill in the art to practice the entire scope of the claimed methods, as of the earliest filing date sought in the instant application. Therefore, this rejection is maintained.

Conclusion

No claim is allowed.

This application contains claims 4-6, 12, and 28-30, drawn to inventions nonelected without traverse in the reply filed on November 7, 2006 and February 27, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
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Art Unit 1635

/J. E. Angell/
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